



UNITED STATES DEPARTMENT OF COMMERCE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/443,070	11/18/99	GILTON	T 3530.2US

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EXAMINER

GABEL, G

ART UNIT

PAPER NUMBER

1641

11

DATE MAILED: 04/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.

09/443,070

Applicant(s)

GILTON, TERRY L.

Examiner

Gailene R. Gabel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 February 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-2, 8, and 12-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claims 1-2, 8, and 12-31 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 18) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 2/8/01 in Paper No. 10 is acknowledged and has been entered. Claims 1, 12-13, 18, and 24-25 have been amended. Claims 30-31 have been added. Claims 1-2, 8, and 12-31 are pending and under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. In light of Applicant's amendment, the rejection of claims 12-13 and 24-25 under 35 U.S.C. 112, second paragraph, is hereby, withdrawn.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-2, 8, 12-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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broader
In this case, the specification does not appear to provide any literal support for the recitation of "said porous capillary substrate comprising a matrix including the same material as said nonporous substrate". Furthermore, none of the originally filed claims recited the limitation in question. Recitation of claim limitation lacking literal support in the specification or originally filed claims constitutes new matter.

not fully encompassed

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-2, 8, 14-16, 18-20, 22-23, and 26-28 stand rejected under 35 U.S.C.

102(b) as being clearly anticipated by Isaka et al. (US 5,482,598) for reason of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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5. Claims 12-13, 21, 24-25, and new claims 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) in view of Sunzeri (US 5,536,382) and Swedberg et al. (US 5,571,410) for reason of record.

6. Claims 17 and 29 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) in view of Northrup et al. (US 5,882,496) for reason of record.

Response to Arguments

7. Applicant's arguments filed 9/27/00 have been fully considered but they are not persuasive.

A) Applicant argues that Isaka does not anticipate the claimed invention because claim 1 recites a separation method that includes applying a sample to an end of a porous capillary column that includes a matrix and at least one capture substrate disposed thereon so that a constituent may be separated from the sample. Applicant further argues that Isaka merely discloses the use of an enzyme which couples to a substrate, only for a sufficient time for the enzyme to catalyze a reaction; thus a chemical change, to the substrate resulting to a detectable change or a measurable detection product. Applicant further argues that Isaka does not disclose that the measurable product is "separated" from the remainder but rather exits the outlet port with the remainder of the sample.

In response, Isaka indeed, reads on what is recited by the claimed invention because the same basic elements and mechanism of “capturing, isolating, and detecting a constituent from a sample” is taught in Isaka wherein the porous matrix functions as a filter to enhance separation of the desired constituent from the sample (see column 4, lines 16-27) and wherein the porous matrix may include a capture substrate, in this case an **immobilized** enzyme, to effect separation based on the affinity of the constituent with the capture substrate. In column 3, lines 10-11, Isaka specifically discloses that “uricase is immobilized in the porous channel to check (by capturing and detecting) the amount of uric acid in serum” in the sample- and the constituent (uric acid) is separated by “capture” of the uric acid analyte by the affinity species (uricase) in the matrix, then the reaction product is detected. Further, the rejected claims do not exclude that the measurable product exits the outlet port of the capillary column with the remainder of the sample but rather only that the capillary column “enhances separation of the constituent from the sample by said at least one capture substrate”.

B) Applicant argues that Isaka does not disclose detecting a constituent with at least one detector disposed proximate a detecting region of the capillary column but instead the constituent and other reaction products exit the column in an outlet port into a capillary for detection.

In response, the specific location of the detector, i.e. proximate a specific (detector) region of the capillary column or along an exit port, is an obvious modification

or variation which routinely varies in the art and which would have constituted an obvious design choice by the Applicant.

C) Applicant argues that claim 18 recites a separation method that includes detecting the binding of a constituent and a stationary phase which is effected at the position where a stationary phase is disposed on whereas Isaka does not disclose “detecting binding” or that binding is detected at the stationary phase of the capillary column.

In response, Isaka et al., indeed, detects binding of an analyte as a constituent and a stationary phase comprising a capture substrate, in this case an enzyme, wherein a chemical change in the constituent is effected by the binding. Moreover, the specific location of the detector for detection is an obvious appropriate modification or variation which routinely varies in the art and which would have constituted an obvious selected design choice by the Applicant. Lastly, with use of the “comprising language”, rejected claim 18 does not exclude that the measurable product exits the outlet port of the capillary column with the remainder of the sample for detection.

D) Applicant argues that Isaka et al. does not disclose “analyzing a detection reagent to determine whether a constituent is present” but rather discloses a fluorescent dye to detect bands during an electrophoretic separation and that the enzyme disclosed in Isaka is not a detection reagent.

In response, Isaka indeed, reads on and anticipates what is recited by the claimed invention because the same basic elements and mechanism of “capturing, isolating, and detecting a constituent from a sample” is taught in Isaka wherein the porous matrix of the column may include a stationary phase, in this case comprising an **immobilized** enzyme, to effect separation based on the affinity of the constituent with the enzyme. In column 3, lines 10-11, Isaka specifically discloses that “uricase is immobilized in the porous channel to check (by capturing and detecting) the amount of uric acid in serum” in the sample- and the constituent (uric acid) is separated by “capture” of the uric acid analyte by the affinity species (uricase) in the matrix, then the reaction product is detected. Moreover, the rejected claims do not exclude that the fluorescent dye is a “detection reagent” since a fluorescent signal by the fluorescent dye is in essence detectable and fluorescent dyes are conventionally used in the art as “label reagents” for measurable products. Applicant's arguments, therefore, fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the reference cited.

E) Applicant argues that the rejection of claims 12-13, 21, 24-25 is improper for reasons that a dependent claim is obvious only if the independent claim from which it depends is obvious. Applicant also argues that the rejection of claims 17 and 29 is improper for reasons that a dependent claim is obvious only if the independent claim from which it depends is obvious.

In response, independent claims 1 and 18 have been rejected on the basis of anticipatory reasons by Isaka et al. The dependent claims that were rendered obvious were not deemed anticipatory by Isaka et al. Therefore, to render obvious a previously rejected claim under an anticipatory 102 (b) rejection would, otherwise, weaken the anticipation rejection. For that reason, claims 12-13, 21, 24-25, and new claims 30-31 are properly rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) in view of Sunzeri (US 5,536,382) and Swedberg et al. (US 5,571,410) with claims 1 and 18 anticipated under 102 (b) by Isaka et al. for reason of record. Likewise, claims 17 and 29 are properly rejected under 35 U.S.C. 103(a) as being unpatentable over Isaka et al. (US 5,482,598) in view of Northrup et al. (US 5,882,496) with claims 1 and 18 anticipated under 102 (b) by Isaka et al. for reason of record.

F) Applicant argues that there is no motivation to combine the teachings of Sunzeri and Swedberg with Isaka because 1) the specific binding partner in Sunzeri is not immobilized to the capillary substrate, but rather the binding elements are prebound, and therefore one of ordinary skill in the art would not be motivated by the teachings or suggestions of Sunzeri to immobilize a specific binding partner to capture the other member, and 2) Swedberg teaches a capillary electrophoresis separation device which includes an open trench formed in a substrate filled with different synthetic porous materials; therefore, one of ordinary skill in the art would not have been motivated to apply the teachings of Swedberg to the subject matter of Isaka.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Additionally, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the rejection is based on the combined teachings of the references as follows. Isaka discloses a method of isolating constituents in a sample using a chromatography apparatus wherein the sample is applied to a first end of the capillary matrix then drawn across a flowfront through the porous matrix channel from the second end by capillary action or, otherwise, by differential pressure. The porous matrix functions as a filter which enhances separation of the desired constituent from the sample and may include a capture substrate wherein separation is on the basis of affinity or absorptivity of the constituent with the capture substrate in a reaction. Sunzeri is incorporated only for his teaching of the benefit of including internal and external standards or controls alongside sample analysis in capillary electrophoresis. Swedberg is incorporated for his teaching of a stationary phase in miniaturized column devices onto which separation and capture functions are combined in a particular matrix such as in an **affinity chromatography**

matrix which specifically includes a variation of selected biological affiants: an antibody, an antigen, a lectin, enzyme etc. to function as the capture species.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the capture substrate in the chromatographic separation apparatus taught by Isaka to include other capture species such as antigens and antibodies, such as taught in the affinity chromatographic matrix of Swedberg in order to achieve enhanced simultaneous performance of separation, filtration, and capture function in a single chromatographic device because Swedberg specifically suggested that a variation of capture species can be incorporated into separation devices to perform such capture function. One of ordinary skill in the art would have been motivated to combine the teachings of Swedberg in incorporating a variation of species into a separation matrix with teaching of Isaka in using porous silicon matrix in a capillary column for separation because Isaka specifically taught the advantage of porous silicon as matrix because of its established porosity which enhances capacity for separation, augments adsorption, differentiates flow rate in samples, thereby producing a highly versatile miniaturized chromatographic device capable of enhanced partitioning and complexation reactions. Furthermore, with the advent of silicon micromachining and LIGA in the teachings of Swedberg, one of ordinary skill in the art would have reasonable expectation of success in fabricating multiple separation columns or channels with a high degree of uniformity and precision in order to allow side by side accurate comparative and correlative measurement of sample results in comparison to internal controls, references, or standards with known measurement levels such as

taught by Sunzeri, because quality control monitoring is standard laboratory practice and a well known art for monitoring the functionality, accuracy, and precision of various laboratory apparatus and methods.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

8. No claims are allowed.

9. Applicant's amendment necessitated the new ground of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday from 7:00 AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

gr Gabel 4/21/01

Gailene R. Gabel
Patent Examiner
Art Unit 1641

Long V. Le

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1800

04/23/01